Claims

What is claimed is:

1. A method of treating a CNS disorder which comprises orally administering to a patient a therapeutically effective amount of lamotrigine or a pharmaceutically acceptable derivative thereof in the form of a sustained release formulation.

2. A method as claimed in claim 1 wherein the lamotrigine or a pharmaceutically acceptable derivative is present in the range of 1 to 500 mg.

3. A method as claimed in claim 1 wherein substantially all the lamotrigine or a pharmaceutically acceptable derivative is released from the formulation in a period of 2 to 20 hours after administration to a patient.

4. A method as claimed in claim 1 wherein the administration is once a day.

5. A method as claimed in claim 1 wherein a reduction in the adverse event profile is achieved.

6. A method as claimed in claim 1 wherein the CNS disorder is selected from epilepsy; pain; oedema, multiple sclerosis or schizophrenia.

7. A method as claimed in claim 1 wherein the CNS disorder is a psychiatric indication.

8. A method as claimed in claim 7 wherein the psychiatric indication is bipolar disorder.

9. A method as claimed in claim 1 wherein the lamotrigine or a pharmaceutically acceptable derivative is present in the range of 1 to 500 mg and wherein substantially all the lamotrigine or a pharmaceutically acceptable derivative is released from the formulation in a period of 2 to 20 hours after administration to a patient.

10. A method as claimed in claim 1 wherein substantially all the lamotrigine or a pharmaceutically acceptable derivative is released from the formulation in a period of 2 to 20 hours after administration to a patient and a reduction in the adverse event profile is achieved.

11. A method as claimed in claim 1 for treating epilepsy; pain; oedema, multiple sclerosis or schizophrenia wherein the lamotrigine or a pharmaceutically acceptable derivative is present in the range of 1 to 500 mg for administration once a day.

12. A method of reducing the incidence of at least one adverse event associated with the administration of lamotrigine or a pharmaceutically acceptable derivative thereof, which method comprises orally administering to a patient a therapeutically effective amount of lamotrigine or a pharmaceutically acceptable derivative thereof in the form of a sustained release formulation.

13. A sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof.

14. A sustained release formulation as claimed in claim 13 wherein substantially all the lamotrigine or a pharmaceutically acceptable derivative thereof is released from the formulation 2 to 20 hours after administration to a patient.

15. A sustained release formulation as claimed in claim 13 which has an *in vitro* dissolution profile in which 40 to 65 % of the lamotrigine is dissolved in 3 to 8 hours.

16. A sustained release formulation as claimed in claim 13 which has an *in vitro* dissolution profile as shown in or substantially similar to any one of Figures 3, 4 or 5.

17. A sustained release formulation as claimed in claim 13 which has an *in vitro* dissolution profile wherein the Area Under the Curve value is between 80% and 125% to that of any one of Figures 3, 4 or 5.

18. A sustained release formulation as claimed in claim 13 which upon administration to a patient has an *in vivo* profile as shown in or substantially similar to Figure 7.

19. A sustained release formulation as claimed in claim 14 which has an *in vitro* dissolution profile in which 40 to 65 % of the lamotrigine is dissolved in 3 to 8 hours.

20. A sustained release formulation as claimed in claim 14 which has an *in vitro* dissolution profile in which 40 to 65 % of the lamotrigine is dissolved in 3 to 8 hours and upon administration has an *in vivo* profile as shown in or substantially similar to Figure 7.

21. A sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof in which there are at least two phases in the release of lamotrigine or a pharmaceutically acceptable derivative thereof, wherein the release rate in the first phase is different from the release rate in the second phase.

22. A sustained release formulation as claimed in claim 13 which has an *in vitro* dissolution profile as shown or substantially similar to that shown in Figure 6.

23. A sustained release formulation as claimed in claim 21 which has an *in vitro* dissolution profile as shown or substantially similar to that shown in Figure 6

24. A sustained release formulation as claimed in claim 13 which has an *in vitro* dissolution profile wherein the Area Under the Curve value is between 80% and 125% to that of Figure 6.

25. A sustained release formulation as claimed in claim 21 which has an *in vitro* dissolution profile wherein the Area Under the Curve value is between 80% and 125% to that of Figure 6.

26. A sustained release formulation as claimed in claim 13 which upon administration to a patient has an *in vivo* profile as shown or substantially similar to that shown in Figure 9

27. A sustained release formulation as claimed in claim 21 which upon administration to a patient has an *in vivo* profile as shown or substantially similar to that shown in Figure 9

28. A sustained release formulation as claimed in claim 13 wherein the formulation is a functional coated tablets or caplets, or time-release tablets or caplets matrices containing wax or polymer, or osmotic pump devices or combinations thereof.

29. A sustained release formulation as claimed in claim 28 which is a matrix tablet.

30. A sustained release as claimed in claim 29 wherein the formulation comprises;

a) 2.5 to 80% by weight lamotrigine or a pharmaceutically acceptable derivative thereof;
b) 10 to 70% by weight release retarding polymer;
c) 0 to 70 % by weight diluent;
d) 0 to 20 % by weight compression aid; and
e) 0.1 to 2.5% by weight lubricants.

31. A sustained release formulation claimed in claim 29 wherein the formulation comprises

a) 8.3 to 50 % by weight lamotrigine or a pharmaceutically acceptable derivative thereof;
b) 17.5 to 66.3 % by weight Methocel E4MP, CR Grade, POLYOX WSRN-80 or Methocel, K100LV or a mixture thereof;
c) 25 to 60 % by weight lactose; and
d) 0.1 to 0.4 % by weight magnesium stearate.

32. A sustained release formulation as claimed in claim 29 which upon administration to a human produce a AUC values of 80 to 125% and a C_{max} being of about 30% less than an instant release tablet containing the same amount of lamotrigine or a pharmaceutically acceptable derivative thereof.

33. A sustained release formulation as claimed in claim 28 which is a DiffCORE tablet.

34. A sustained release formulation as claimed in claim 13 comprising

1) a core comprising lamotrigine or a pharmaceutically acceptable derivative thereof:

2) an outer coating covering said core, the thickness of said outer coating being adapted such that it is substantially impermeable to the entrance of an environmental fluid and substantially impermeable to the exit of lamotrigine or a pharmaceutically acceptable derivative thereof, and

3) said outer coating including one or more orifices extending from the outside of the coating substantially completely through said coating but not penetrating said core allowing the release of lamotrigine or a pharmaceutically acceptable derivative thereof from the core into enviromental fluid, said orifices having an area or combined area from about 10 to about 60 percent of the face area of said formulation, wherein the release lamotrigine or a pharmaceutically acceptable derivative thereof occurs substantially through said orifice.

35. A sustained release formulation as claimed in claim 34 wherein the release of lamotrigine or a pharmaceutically acceptable derivative thereof is via one or more of dissolution, diffusion osmosis or erosion

36. A sustained release formulation as claimed in claim 34 wherein the core further comprises a release retarding excipient.

37. A sustained release formulation as claimed in claim 34 wherein the outer coat may dissolves by 0.3 to 5 hours after administration or when the surrounding pH exceeds 5.

38. A sustained release formulation as claimed in claim 34 wherein the formulation comprises a core comprising

a) 2.5 to 80% by weight lamotrigine or a pharmaceutically acceptable derivative thereof;
b) 17.5 to 70% by weight release retarding polymer;
c) 0 to 60 % by weight diluent;
d) 0 to 20 % by weight compression aid; and
e) 0.1 to 2.5% by weight lubricants and

an outer coat comprising

f) 0.05 mm to 0.30 mm of polymer.

39. A sustained release formulation as claimed in claim 13 wherein the formulation comprises a core comprising

a) 2.5 to 80% by weight lamotrigine or a pharmaceutically acceptable derivative thereof;

b) 17.5 to 70% by weight release retarding polymer;

c) 0 to 60 % by weight diluent;

d) 0 to 20 % by weight compression aid; and

e) 0.1 to 2.5% by weight lubricants and

an outer coat comprising

f) 0.05 mm to 0.30 mm of polymer.

40. A sustained release formulation as claimed in claim 38 wherein the outer coat may dissolves by 0.3 to 5 hours after administration or when the surrounding pH exceeds 5.

41. A sustained release formulation as claimed in claim 39 wherein the outer coat may dissolves by 0.3 to 5 hours after administration or when the surrounding pH exceeds 5.

42. A sustained release formulation as claimed in claim 34 which upon administration to a human produce AUC values outside the range 80 to 125% and a C_{max} being of about 30% less than an instant release tablet containing the same amount of lamotrigine or a pharmaceutically acceptable derivative thereof .

43. A method of achieving a serum concentration wherein upon administration to a patient of a sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof produces area under the curve values of 80 to 125% and a C_{max} being of about 30% less than an instant release tablet containing the same amount of lamotrigine or a pharmaceutically acceptable derivative thereof.

44. A method of achieving a serum concentration wherein upon administration to a patient of a sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof produces area under the curve values outside the range of 80 to 125% and a C_{max} being of about 30% less than an instant release tablet containing the same amount of lamotrigine or a pharmaceutically acceptable derivative thereof.